Clinical Proceedings

of the

CHILDRENS HOSPITAL

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SHOULD VITAMIN D BE GIVEN ONLY TO INFANTS?

VITAMIN D has been so successful in preventing rickets during infancy that there has been little emphasis on continuing its use after the second year.

But now a careful histologic study has been made which reveals a startlingly high incidence of rickets in children 2 to 14 years old. Follis, Jackson, Eliot, and Park* report that postmortem examination of 230 children of this age group showed the total prevalence of rickets to be 46.5%.

Rachitic changes were present as late as the fourteenth year, and the incidence was higher among children dying from acute disease than in those dying of chronic disease.

The authors conclude, "We doubt if slight degrees of rickets, such as we found in many of our children, interfere with health and development, but our studies as a whole afford reason to prolong administration of vitamin D to the age limit of our study, the fourteenth year, and especially indicate the necessity to suspect and to take the necessary measures to guard against rickets in sick children."

*R. H. Follis, D. Jackson, M. M. Eliot, and E. A. Park: Prevalence of rickets in children between two and fourteen years of age, Am. J. Dis. Child. 66:1-11, July 1943.

MEAD'S Oleum Percomorphum With Other Fish-Liver Oils and Viosterol is a potent source of vitamins A and D, which is well taken by older children because it can be given in small dosage or capsule form. This ease of administration favors continued year-round use, including periods of illness.

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FOREWORD

Joseph S. Wall, M.D. Chairman,
Medical Staff

THE founding fathers of the Children's Hospital possessed the sagacity and foresight to name as one of the objects of the hospital the function of education. The first article of the constitution adopted in 1870 stated the following three objectives of the institution:

1. The medical and surgical treatment of sick children.
2. Instruction in the diseases of children.
3. Instruction of young women in the duties of nursing.

This early recognition and designation of teaching as a function almost coequal, certainly at least coordinate, with the treatment of sick children has characterized the work of our hospital from its very inception up to the present day. In recent years, owing to the rapid modern advances in both medical and surgical knowledge, diffusion of such knowledge of the ailments of children together with the latest concepts of treatment, has been of even greater urgency in order that the greatest good might be accomplished, both by better equipment of the physician, and in turn, a wider application of this skill for the benefit of sick children.

As a means toward this end, the hospital has conducted in recent years more frequent group clinical conferences or consultations open to and attended by all members of the Attending and Resident Staff of physicians, nurses, and individuals forming the hospital personnel. Such conferences are held twice weekly with one staff luncheon conference once a month.

During these assemblies, all varieties of illness affecting our children, common and usual as well as the rare and unusual, are brought forward for discussion. Should the condition of the patient permit, the child is examined in the conference room by several members of the Staff thereby receiving the benefit of the consultative concensus of many experienced minds which in many instances determines the successful treatment of the ailment in question.

It must be borne in mind that these conferences are formulated, the titles for discussion prepared, and the presentations conducted by members of the Resident Staff to whom must be accorded the credit for their success and which in turn is dependent entirely upon

the eagerness and diligence which our Residents have constantly shown in their development.

For a long time, many members of the Attending and Resident Staff have felt that a great deal of instructive and useful knowledge elicited through the medium of the conferences has been unavoidably lost because of the failure to properly record and preserve in permanent form for future study and reference the valuable lessons gleaned from the interchange of opinion incident to the medical discussion during the consultations.

Upon the initiation of the Resident Staff and entirely through their own efforts, arrangements have been made to publish in bulletin form the material emanating from the clinical conferences. There can be no question of the enormous advantage of so preserving in printed form a journal of these reports which will be prized not only by those in attendance upon the clinics, who have had the good fortune to actually hear and participate in the discussions, but by a wider circle of the less fortunate who were not present but may reap the benefit of discussions through the medium of the printed word.

Of particular interest to our many graduate Residents, some in the far off corners of the world, will be their ability to keep in touch with the activities of their Alma Mater in which they once eagerly participated.

To the Editors and Associate Editors of the Resident Staff who must receive the credit for the initiation of this worthy project, and whose shoulders must bear the not inconsiderable burdens of carrying on this publication, the Medical Staff pledges its support and extends its sincere felicitations.

CASE REPORT NO. 1

ATRESIA OF THE ESOPHAGUS WITH TRACHEO-ESOPHAGEAL FISTULA

Dr. Frederic G. Burke C. D. (44-3267)

A forty-eight hour old white female admitted to the Hospital on September 26, 1944 with the chief complaint of vomiting all feedings, excessive salivation and paroxysmal attacks of cyanosis. This infant was born two days before, in Sibley Hospital, after a normal labor and delivery. Immediate vomiting resulted following the first attempt at feeding, and subsequent efforts to feed provoked the same response. An attempt to pass a catheter into the stomach revealed an obstruction, and the diagnosis of atresia of the esophagus was made. The infant weighed 7 lbs. 6 ozs. at birth and upon admission, appeared to be in moderate respiratory distress.

Physical examination revealed a large amount of mucus in the throat due to excessive salivation. There were numerous moist rales, elicited throughout both lung fields. The heart was normal, as was the remainder of the physical examination.

A soft rubber catheter was dipped in Lipiodol solution and passed into the esophagus under the flouroscope to the point of obstruction. Two cc. of Lipiodol was then instilled through the catheter and x-rays of the cervical region and thorax were taken in the anterior-posterior and lateral positions. These roentgenograms revealed the opaque material to be accumulated in an esophageal pouch in the region of the seventh cervical vertebra. The presence of air in the stomach confirmed the existence of an esophageal tracheal fistula somewhere below this pouch. The infant was given sodium sulfadiazine, grains 10 q.d. for prophylactic purposes against pneumonia. Her temperature upon admission was 97.2° and rose to 100.2° that same day after employment of a heat cradle. The following day her temperature was 101° but subsequently was normal. Her weight upon admission was 14 ozs. less than birth weight, and by the use of glucose, plasma and Amigen* clyses, rose to 7 lbs. 1 oz., before operation by Dr. Davis and Dr. Klepser, twenty-four hours later. Aspiration of the nose and throat was carried out every 2-5 minutes and oxygen was employed intermittently for cyanotic spells which resulted from occasional aspiration of excessive secretions. The culture of the secretions revealed numerous streptococci viridans. Her preoperative condition was described as fair and, im-

*Amigen—(Casein Hydrolystate—Amino Acid Solution, Mead-Johnson Co.)

mediately following the operation, she received 75 cc. of whole blood. An examination of the blood before operation revealed the hemoglobin to be 15 gms., red cell count 5,300,000, white cell count 5,200, with 49% neutrophiles, 49% lymphocytes, and 2% eosinophiles.

Following the first stage of this operation the patient received the same supportive subcutaneous therapy. Her temperature remained normal and her weight curve was maintained. Four days afterwards, the second stage, a gastrostomy was performed without complication. Frequent aspiration of the nose and throat was continued and after twenty-four hours, small amounts (½ drams each) of 5% glucose and normal saline were given by mouth and aspirated from the cervical stoma. Similar amounts were introduced into the stomach through a projecting catheter. A dram each of 10% amigen and 5% glucose was substituted for the stomach feeding at two hour intervals and half the daily subcutaneous clyses were omitted. Sixty hours following gastrostomy, a weak lactic acid, evaporated milk formula was introduced at three hour intervals into the stomach by means of a syringe, ten to fifteen minutes being taken for each feeding. The capacity was gradually increased from 1 to 2½ ozs. and evidence of fullness was noted by leakage at the site of the gastrostomy. Irritation due to this leakage was counteracted by boric acid ointment around the stoma. Five days after gastrostomy all clyses were discontinued and her weight maintained by the formula alone. Twelve days after admission her weight was 7 lbs. 12 ozs., an increase of one lb. 4 ozs. A pacifier is employed empirically during the time of her artificial feeding, with salutary relief from crying, and small amounts of amigen and glucose solution were given by mouth to stimulate taste bud development and central reflexes.

Subsequent roentgenographic examinations of the chest have failed to reveal any evidence of pathology of the parenchyma and the infant seems to be progressing nicely.

DISCUSSION—Dr. Edgar Davis

Dr. McLendon called me in consultation on September 25, 1944. The baby was then 24 hours old. Dr. McLendon had already made the diagnosis clinically. We agreed that inasmuch as the baby's general condition was satisfactory, it would be best to transfer the baby to Children's Hospital where fluids, amino acids, blood, etc., could be given.

Courtesy of the X-Ray and Photography Department, Children's Hospital

C. D.—LATERAL VIEW SHOWING LIPIODOL IN THE ESOPHOGEAL POUCH

On September 27, 1944, the baby weighed 7 pounds, 1 ounce, a gain of nine ounces. Her general condition was believed to be fair. An x-ray of the chest showed no evidence of pulmonary infection. Physical examination, however, revealed numerous rales scattered

throughout both lung fields. There was no impairment to percussion. An operation was advised. My operative note was as follows:

"She was placed on her right side. Because of a previous infusion, just prior to the operation, the subcutaneous tissue and skin were so edematous that it was impossible to locate the spinous processes or the vertebral border of the scapula. This made it rather difficult to know exactly where the incision was being placed. An attempt was made to make a peri-scapular incision from the 2nd rib posteriorly, extending downward between the scapula and the spine to the lower border of the scapula and thence passing downward and anteriorly to about the 6th rib. The sacrospinalis muscle was extremely broad, being attached a little further outward than the curve of the rib. About 4 cm. of the 5th and 4th ribs and about 3 cm. of the 3rd and 2nd ribs were resected subperiosteally. A very nice cleavage plane was found easily through the endothoracic fascia. An extra pleural separation was carried to the mediastinum without incident. The arch of the aorta, the left vagus nerve and the subclavian artery were easily identified. The end of the esophagus communicating with the posterior wall of the trachea was identified easily, but was separated with moderate difficulty. After getting the esophagus free, it was found to communicate with the posterior wall of the trachea at the carina rather than the usual position somewhat above the carina. A single silk ligature was applied around the esophagus next to the trachea. A search was then made for the upper blind end of the esophagus. This could not be found until the anesthetist inserted a small soft rubber catheter through the mouth into the esophagus. With gentle pressure on the catheter by the anesthetist, the blind pouch could barely be seen. The lower end of the pouch was then grasped with an Allis clamp and it was freed from the surrounding structures. The entire length of this pouch was not more than one half an inch. Two fine silk sutures on full curved baby Emmett round needles were inserted into this pouch and were clamped with hemostats to facilitate subsequent identification. The end of the esophagus joining the trachea was then divided just distal to the silk ligature which had been applied previously. It was then found that the lower end and the upper end of the esophagus could not be brought together, there being a total absence of the esophagus for a distance of about 3 cm. This precluded any possibility of a direct anastomosis. A fine silk ligature was then tied around the esophagus very loosely. The end of the esophagus was closed with a Lembert suture of fine silk. It was then released and returned to its normal position. A short 2½ cm. incision was made through the skin of the left side of the neck about three-fourths of an inch above the clavicle. The sternal and clavicular part of the sterno-mastoid muscle were separated and by blunt dissection the trachea and the upper end of the esophagus were exposed without difficulty by retracting the corotid sheath laterally. A forcep was inserted downward into the extra-pleural space and the two silk threads which had been previously anchored into the wall of the blind upper end of the esophagus were grasped and drawn out through the base of the neck. It was then discovered that the esophageal pouch was so short that it did not reach the skin surface without tension. The pouch was then anchored to the superficial layer of the cervical fascia, the platysma muscle and the skin. Several sutures were necessary to anchor the pouch securely to avoid retraction into the deeper structures. The end of the pouch was opened so as to permit escape of pharyngeal secretions externally. A small dressing was applied. Before closing

the muscle layer, a soft rubber catheter was inserted into the extra-pleural space and constant suction was applied. No drain was inserted."

Pharyngeal secretions promptly began escaping through the upper end of the esophagus out onto the chest. These secretions were aspirated from time to time, but much less frequently than was necessary preoperatively. The night following the operation, the baby nursed her thumb frequently and was given a rubber nipple to pacify her. Medical management was continued by or under the supervision of Drs. McLendon and Burke.

October 1, 1944, the baby weighed 7 pounds, 3 ounces. This was the fourth postoperative day. An x-ray of the chest had been made daily which showed no evidence of pulmonary infection. It was believed the baby was in the best possible condition for the second operation. My operative note is as follows:

"A 3 cm. paramedian incision was made from the costal margin a short distance to the left of the midline. The anterior rectal sheath was opened. The muscle fibers were retracted laterally. The peritoneum was opened. The liver was very large and extended about 3 cm. below the lower end of the incision. None of the viscera could be seen except the liver. Gentle retraction on the left side of the wound was made and a vein retractor was inserted through the wound and very gently hooked over the edge of the liver. The liver was then drawn toward the right and upward. This brought into view the stomach. The stomach was then gently grasped with a Babcock forcep and was brought up into the wound. The highest place on the anterior surface of the stomach in the fundus was selected. A number 28 urethral soft rubber catheter was inserted into the stomach and anchored securely with three purse string sutures. The stomach was anchored to the peritoneum and the fascia with several catgut sutures. The wound was then closed in layers in the usual manner without drainage. A clamp was applied to the upper end of the rubber tube."

The diagnosis of congenital atresia of the esophagus can be easily, safely, and definitely made.

The tip of a soft rubber catheter, 10 or 12 French, is dipped into Iodochloral or 40% Lipiodol. Under fluoroscopic observation the catheter is passed through the baby's mouth into the esophagus. The iodized oil which clings to the catheter makes it readily visible under the fluoroscope. X-rays can then be taken with the catheter in situ which will show the catheter extending as far downward as the upper pouch of the esophagus extends. It is not necessary to insert Lipiodol into this upper blind pouch, but if desired, only 1 or 2 cc. is necessary. The catheter can then be withdrawn and x-rays taken. The catheter is then reinserted into the esophagus and the oil is aspirated. The use of iodized oil in sufficient quantity to flood the tracheo-bronchial tree and admit oil into the stomach through

the tracheo-esophageal fistula is unnecessary, dangerous and is strongly condemned.

If an air bubble is visualized in the stomach by x-ray, tracheo-esophageal fistula is obviously present. Presumably, the air from the trachea enters the stomach when the baby cries which increases the intrapulmonary pressure.

Congenital atresia of the esophagus does not, to casual inspection, present any characteristic evidence at birth. Usually cyanotic spells and accumulation of mucus occur at intervals during the first day or so after birth which necessitate resuscitation. When feeding is first started there is always coughing and regurgitation, and respiration becomes alarmingly difficult associated with cyanosis. These symptoms should always lead a careful nurse, the pediatrician, the obstetrician, or the physician in charge to suspect that this condition exists. The baby should then be studied to ascertain the presence or absence of esophageal anomaly before any further attempt is made to feed the baby. Subsequent attempts to feed the baby with esophageal atresia inevitably leads to aspiration pneumonia, dehydration, and death. Distention of the stomach with gas, due to passage of air through the tracheo-esophageal fistula has not been a prominent symptom in my experience.

If untreated surgically, death is inevitable, usually within the first ten days. Surgery is designed to: 1) prevent pneumonia by aspiration of pharyngeal secretions: 2) prevent pneumonia by regurgitation of gastric contents through the fistula: and 3) furnish nutrition. A gastrostomy alone should never be done as a preliminary step. Dr. George Humphries from the Babies Hospital at Columbia University, New York city, demonstrated that introduction of iodized oil through a gastrostomy tube would visualize not only the stomach, but also the tracheo-bronchial tree and the upper end of the esophagus. Therefore, gastrostomy alone does not permit safe feeding, neither does it prevent pneumonia by regurgitation or by aspiration.

The prevention of pneumonia is the most urgent objective. Pharyngeal secretions which are usually very abundant must be aspirated frequently. If the anatomical structures permit, a direct anastomosis of the upper and lower ends of the esophagus is the preferable procedure. Haight states that if there is an absence of more than 1 cm. of the esophagus, an anastomosis is not likely to be successful because, even though the anastomosis may be possible, there will be so much tension on the suture line that leakage is

almost inevitable. In this case there was an absence of 3 cm. Prevention of pneumonia was possible by: 1) disconnecting the esophagus from the trachea, closing the esophagus and its opening into the trachea: and 2) drawing out through the base of the neck the upper blind pouch of the esophagus and opening of this pouch to permit escape of pharyngeal secretions externally. The third objective, namely nutrition, was accomplished four days after the first operation by a simple gastrostomy.

Seven days after the last operation, the baby weighed 7 pounds, 12 ounces, which represented a gain of 9 ounces in six days. The chest wound healed nicely. There was some leakage of the formula, around the gastrostomy tube, but minor adjustments permitted satisfactory feeding. Frequent x-rays of the chest have shown in every instance clear lung fields. There has been no accumulation of fluid in the extra pleural space.

The last check-up on November 2, 1944, showed the infant to have progressed well and uneventfully. She has gained 1 pound, 8 ounces since admission. She has been fed a little orange juice, lemon juice, etc., by mouth several times daily since the first operation at three days of age to prevent salivary stagnation and to develop taste buds. She swallows easily and the liquids are immediately expelled onto the chest.

We later contemplate construction of an ante-thoracic esophagus.

A REPORT ON THE USE OF PENICILLIN AT CHILDREN'S HOSPITAL

—John Washington, M.D.

This report includes approximately the last fifty cases treated with penicillin at The Children's Hospital. The routine method of administration has been by intramuscular injection every three hours. The solution used contains 5000 units per cc. The average dose was 10,000 units or 2 cc., every three hours. For infants this was cut to 5,000 units; for large children or critically ill children, 15,000 unit doses were often used. Initial doses of 30,000 units usually were given.

In meningitis five to fifteen thousand unit doses have been

References:
1. Haight, *Personal Communication.*
2. Humphreys, G. H. II., *The Surgical Treatment of Congenital Atresia of the Esophagus, Surgery* 15:5 (May 1944).

given intrathecally. The only reactions to the drug, which have been noted, occurred in the subarachnoid space where the spinal fluid cell count has been observed to increase after repeated injections.

Solutions are made simply by injecting 20 cc. of sterile distilled water through the rubber stopper of a vial containing 100,000 units of powdered penicillin.

PNEUMONIA

Three cases of pneumonia were treated. One was two months old with broncho-pneumonia associated with pertussis. Streptococcus viridans seemed to be the invader. There was no response to sulfathiozole. Penicillin therapy received an excellent response.

The second was critically ill with bilateral pneumonia on top of a severe anemia of the sickle cell variety. Pneumococcus and streptococcus viridans were cultured. The response to penicillin was good. Sulfa drugs were not given.

The third was a thirteen year old with pneumonia of seven days duration which did not respond to sulfa therapy. There was a response by lysis to penicillin. The order for a sputum culture was written but never checked off.

One case of post-tonsillectomy atelectasis was treated with subsiding of fever and resolution of a triangular area of density at the cardio-phrenic angle.

MENINGOCOCCIC MENINGITIS

The sulfa drugs are so effective in this disease that penicillin must produce miracles to supplant them. If penicillin will combat meningococci faster than sulfadiazine, then some additional patients with acute overwhelming infections may be saved.

Eight cases are included in this review. Two of them are quite young, four and six months respectively, and were offered penicillin's possible added support because their ages made their prognosis less good. The other six cases ranging in age from one year to twelve years were judged quite ill on admission. Descriptions of their appearances vary from very ill, to coma, or to delirium with question of the Waterhaus-Fridreichsen syndrome. All received routine doses of sulfadiazine as well as penicillin. Penicillin was given at least once intrathecally, in addition to the usual intramuscular injections at three hour intervals. The only certain statement that can

be made about the series is that all recovered. In reviewing the charts it seemed to me that recovery was possibly more prompt.

Spinal fluid cultures were regularly negative on the second or third day. As I recall, this same prompt sterilization occurs pretty regularly when the sulfa drugs alone are used.

One occurrence of interest was a second rise in the spinal fluid cell count, presumably due to reaction to the intrathecal injections of penicillin. This was most marked in the four month old baby whose count on admission was 2,130 cells; on the fourth day it was down to 300; and on the fifth, back to 2,200—80 per cent polys. He was getting fifteen thousand units daily intrathecally. This was stopped and the count rapidly subsided. I believe that Dr. Rice now considers 15,000 units an excessively large dose for the subarachnoid space.

The question of how long to keep up the penicillin naturally arises. I believe Dr. Rice is inclined to stop it when the patient seems out of danger, depending on the continued sulfa therapy to complete the cure.

Three cases of pneumococcus meningitis have been treated. One aged five months, one fourteen months, and one seventeen months. All survived. But, unfortunately, the 14 month old child sustained permanent brain damage.

The real triumph is, of course, the five months old infant. He received (in addition to penicillin) sulfadiazine and type 28 antiserum,—i.m. The spinal fluid on admission was turbid with organisms, the count being only 380 cells. The culture was taken on the fourth day with a count of 50 cells. The temperature was normal on the seventh day. The sulfa drugs have saved many children with pneumococcus meningitis but very few less than one year of age.

Dr. Cassidy, I believe put in a good many extra man hours treating this baby. The baby recovered completely and was readmitted just the other day with diarrhea.

This series is, of course, too small to draw any conclusions although three recoveries in a row is good.

The seventeen month old child was shown here several weeks ago. Dr. McLeod questioned the diagnosis because the spinal fluid cell count was never above 533; however, pneumococci were obtained on culture twice. There was no response to sulfa therapy and apparently never to i.m. penicillin. After an intrathecal injection of 5,000 units, the temperature dropped sharply to normal and stayed there. It may have been a coincidence, of course.

An article in the J.A.M.A. of Oct. 7, 1944 stated that, although penicillin did not pass from the blood stream to the spinal fluid in a well person, it was found to make the passage when the meninges were inflamed. If the intrathecal injection in the above patient did cure him, after i.m. injection failed, it would appear that in this patient the passage of penicillin was not made in the presence of meningitis. On the other hand, with only 500 cells in the spinal fluid it would be argued that the inflammation of the meninges was too minimal to cause the abnormal passage of the drug.

GONORRHEA

One case of gonorrhea was treated. This was vaginitis in a seven year old girl. It had resisted sulfa therapy. Two days of i.m. penicillin treatment seemed to cure it. As you know, sulfa therapy has been quite effective in vaginitis and, except in sulfa resistance cases, penicillin probably will not supplant it if the latter treatment requires hospitalization. On the other hand, if penicillin can be counted on to act so promptly, it might be argued that it is better practice to hospitalize for a few days on the grounds that secondary cases in the family would be eliminated.

CHRONIC OSTEOMYELITIS

Only one case of chronic osteomyelitis is included. This was an eleven year old child with disease of the tibia. The involved bone was saucerized and 1,560,000 units of penicillin administered in two post operative weeks. There was still some drainage when the patient was discharged.

FURUNCULOSIS

Three cases of furunculosis were treated very successfully. In one there were multiple abscesses of the scalp in a 4½ month old baby following x-ray treatment of an hemangioma. There was considerable cervical adenitis. Such a condition at 4½ months ordinarily would have been highly dangerous, although the sulfa drugs might have controlled it. After three days of penicillin therapy there was subsidence. Another 17 month old baby was cured of multiple small abscesses of the face in six days. The third was a most interesting seven months old boy who developed severe furunculosis on top of severe eczema. The furunculosis did not respond to sulfa therapy. He did not seem too ill but blood culture showed many colonies of staphylcocci. Penicillin was

of staphylococcus to count. The blood became sterile and the abscesses cleared beautifully. The penicillin was discontinued and in one week a few new abscesses appeared and again the blood culture showed many colonies of staphylococci. Penicillin was again given, this time for two weeks. When stopped the sepsis recurred a second time. The final penicillin course lasted for over three weeks, the injection being given at longer and longer intervals towards the end. He is now free of the staphylococcus, so far as is known.

SEPTICIMIA

A seven year old with post scarlet fever strep. hemolyticus septicimia responded promptly to penicillin (after sulfa therapy, strangely, had failed completely).

NEPHROSIS

What promises to be an important although limited use for penicillin is the treatment of the infections which beset edematous children suffering from nephrosis. If these children can survive bouts of peritonitis and sepsis (most often pneumococcal) they have a good chance of survival, as long as signs of glandular diseases are absent or minimal. One never feels easy using the sulfa drugs because of the danger of further kidney damage. Two such patients have been treated. One, aged two, was admitted moderately sick with temperature of 103° without signs of peritonitis or other explanation for the fever. Penicillin was started—the temperature dropped. The blood culture was sterile. It is impossible to say what, if anything, penicillin contributed. The second child, aged seven, was already on the ward when he developed signs of acute peritonitis and was started on penicillin. He died thirty hours later without showing any response to the drug. Culture showed the offending organism to be the colon bacillus, which accounts for the failure, of course.

EMPYEMA

Not enough empyema has been treated to enable one to draw any conclusions. Only three cases are listed. In two, penicillin was used entirely as an adjunct to surgery and started at the time of operation.

In the third, which was due to streptococcus in a four year old girl, penicillin was given for six days intramuscularly and once into

the chest cavity. She did not respond, and drainage was done later (three weeks). I hope we will have more chance this winter to catch empyema early while the pus is thin, and treat more intensively by injecting the drug repeatedly into the cavity. Some cases of empyema in children will recover simply by repeated aspiration and with no drug as Brennemann pointed out some years ago. It seems likely that treatment by aspiration in junction with injection of penicillin will give better results.

LARYNGO-TRACHEO-BRONCHITIS

One of the most serious diseases of children is laryngo-tracheo-bronchitis. Before the days of the sulfa drugs it was highly fatal. I have the impression that the sulfa drugs have lowered the mortality considerably. Of the three cases treated with penicillin, two had had sulfa therapy without recovery although none was in extremis. All three recovered, the temperature descending by lysis. Streptococcus viridans was cultured from one, streptococcus hemolyticus from one and influenza bacillus from the third. Theoretically, of course, penicillin did not contribute to the recovery of the one infected with the influenza bacillus.

DEEP ABSCESSES

Probably the most important field of all for penicillin is in treating deep abscesses and cellutitis, with or without bone involvement. Its importance here lies, to a great extent, in the fact that the staphylococcus figures prominently. We have seen the staphylococcus defy sulfa therapy too often.

Fourteen such cases are listed. In seven, incision and drainage was necessary on the first, second or (in one case) the third day of therapy. In none of these seven was the drug started before the fourth day of the disease. Whether starting it earlier would have prevented suppuration, of course, is impossible to say. It was used more in support of surgery and was generally thought to have hastened healing. Diagnoses were: Abscess of the arm with questionable involvement of the humerus, parotitis (ten days old), cellutitis of the face and neck, cellutitis of the lower eyelid, adenitis of the neck, submental abscess and prepatella bursitis. The first five were caused by the streptococcus and the remaining two, by the staphylococcus.

Now we come to the seven which did not suppurate. Of course, they might not have done so without penicillin.

(1) Ten years old: Staphylococcus abscess of arm already opened. Metastatic cellutitis of the leg (possibly involving bone). With penicillin, subsided in two and one-half days.

(2) Three years old: Cellulitis of face and neck. Penicillin started third day; cured in four days.

(3) Three years old: Cellulitis of cheek of two days duration; cleared in six days.

(4) Two years old: Cellulitis about a draining osteomyelitis wound; subsided in three days; sinus continued to drain.

(5) Eleven years old: Flareup of osteomyelitis of tibia dormant for one year. Swelling subsided after twelve days of penicillin.

(6) Ten years old: Acute osteomyelitis of tibia following trauma: never any x-ray evidence; ten days duration; subsided with four and one-half days of penicillin.

(7) Fourteen months old: Staphylococcus albus hemolyticus bursitis; drained. Bacteremia was present. Acute osteomyelitis of lower femur with x-ray evidence. Kept on penicillin three weeks. Fever down in ten days. Acute stage over on fourth day. Apparently healed.

Of course, these deep infections even with osteomyelitis sometimes heal with the sulfa drugs. So, for that matter, the role of penicillin might be questioned. However, I believe in these last seven cases the responses were quicker and more consistent than with the sulfa drugs. It appears that if penicillin is started in the first two or three days, suppuration will probably not occur in staphylococcus infections.

The problem arises as to what cases are to be selected for this rather strenuous but at the same time seemingly safe therapy. One wouldn't want to treat every incipient boil, but certainly infections of the face which threaten the cavernous sinus and suspected infections of bone deserve it as soon as they are admitted.

When one considers how long hospital beds are occupied by many cases of even lymphadenitis, it may well turn out to be more economical to treat freely and early with penicillin, than to wait to see what is going to happen with other therapy.

OTITIS MEDIA

Another most interesting field for the use of penicillin is in middle ear disease and mastoiditis. Of course, the sulfa drugs

have been unbelievably effective in this field, but a few failures for one reason or another, turn up.

Six cases are listed. The sulfa drugs had failed to cure the first five. The sixth developed leucopenia with sulfa therapy.

1. Twenty months: duration—fourteen days, ear dry in four days.
2. Six years: duration—twenty-one days, ear dry in five days.
3. Four years: duration—five days (with early mastoiditis) ear dry in four days.
4. Eight months: duration—thirty days, treated three and one-half days, slight drainage persisted.
5. Two years: duration—ninety days. Treated fifteen days with 1,300,000 units. Mastoidectomy then performed, after which, drainage stopped.
6. Eight years (the one with leucopenia): duration—seven days, cured promptly.

From this too small series it would seem that good results can be expected in cases where sulfa therapy fails. The outstanding failure was where the disease had lasted for three months. The finding of a staphylococcus may account for the failure of sulfa drug therapy. It would seem reasonable, in all cases which fail to respond promptly to sulfa therapy, to determine whether a staphylococcus is present and proceed with penicillin before the disease becomes too entrenched in the mastoid.

DISCUSSION: Capt. Monroe Romansky, U.S. Army, Walter Reed Hospital

Regarding the question of intra-thecal administration of penicillin, we have noted that any strength above 10,000 units will produce a pleocytosis of the spinal fluid. Penicillin will persist in the subarachnoid space for as long as seven days, being absorbed from this space very slowly.

In the treatment of gonorrhea, the feasibility of ambulatory penicillin therapy appears very promising. We have been experimenting with penicillin combined with oil in the treatment of this, and other diseases, for the past several months. Approximately 150 cases of gonorrhea have been given a single dose of 150,000 units, combined with oil, intramuscularly, with remarkable success. Cultures were taken from the urethra along with smears every

hour after the injection, and nearly all were negative in three to seven hours. All cases were in males and were of the acute variety. From our preliminary evidence, it would seem that ambulatory treatment of gonorrhea is just around the corner.

I have treated seven cases of impetigo in infants, giving 1,000 units per pound of weight in a single injection, and all were cleared almost miraculously in seven to eight hours.

Furunculosis has also proven amenable to the single injection treatment of penicillin. In deeper abscesses, where there is considerable granulation tissue over the abscess, it has been necessary to simultaneously aspirate by means of a needle and, occasionally, incise and drain the larger pockets of pus, but all of our cases so far have responded very well.

An interesting side action to the single injection treatment has been the complaint of local pain at the site of the infection. This may be indicative of piling up of the dead bacteria.

In the ordinary method of administering penicillin, by repeated single injections, the blood level is a very spiked affair, rising in the first few minutes to excessively high levels, and falling rapidly after the first hour. It is difficult to find any essable amount present at the end of two hours. This rapid absorption and rapid excretion may well explain the fact that penicillin, in the ordinary doses, does not pass to the subarachnoid space.

We have used, as a vehicle, peanut oil with one to three percent beeswax for single shot therapy. It is amazing that such a small amount of beeswax can hold, in solution with the peanut oil, relatively huge amounts of penicillin. It is possible with one percent beeswax to combine 250,000 units of penicillin (sodium) in 1 cc. Because of the hygroscopic quality of the sodium salt, it is probably more practical to use the calcium salt in the preparation of small amounts. The absorption of moisture from the air to the sodium salt, often times causes a somewhat coarse admixture. This property is lacking in the calcium preparation and is, therefore, probably more practical in preparing small amounts. The penicillin level obtained in the blood stream following a single large dose is much more prolonged, a therapeutic level being obtained usually for twelve hours, and often for eighteen hours and longer.

We have treated empyema, roughly 100 cases, and all we can say is that these patients do better with this treatment. However, surgical drainage has been necessary in all of our patients, and so we are not too optimistic.

Dr. Wall: "Have you noted any cases of sensitivity to peanut oil?"

Dr. Romansky: "I have had two cases that were allergic to peanut oil, but this was only manifested by minor symptoms. Curiously, both these patients reacted negatively to a patch test for peanut oil and beeswax. Of course, this might be a reflection upon our technique for determining sensitivity. We do not believe that the few cases that might be sensitive constitute, in any way, a contraindication to the use of penicillin and oil."

Question from the floor: "Have you treated any cases of syphilis?"

Dr. Romansky: "Yes, we have a series, but as yet there are too few in number to justly draw any conclusions.

Question from the floor: "Have you treated any sulfon resistant infections of the urinary tract?"

Dr. Romansky: "We have treated a few cases of proteus and streptococcus fecalis infections and, by giving large doses, have obtained fair results. Concentrations of penicillin in the urine in these cases have been as high as 10,000 units per cc."

CLINICO-PATHOLOGICAL CONFERENCE

Directed By — Dr. E. Clarence Rice
Assisted By — Dr. John E. Cassidy

Held Every Tuesday Afternoon at 3:00 P.M.

CASE REPORT #2

Dr. Tom Wilson

J. K. (44-2277), aged four and one-half years, female, white. Admitted 4-12-44—discharged 5-5-44. Readmitted 5-16-44—died 6-18-44.

CHIEF COMPLAINT

Pain and limping in left leg with pain and aching in neck.

FIRST ADMISSION

PRESENT ILLNESS

About two weeks before admission, patient's mother noticed that the child began to limp and complain of pain in the left lateral

thigh. This condition was aggravated when the thigh was touched and was more marked during the evening. Three days before admission there was pain present in the neck. Appetite had been poor since the onset and she frequently cried. Fever was present and hovered between 101° to 103° at night, and usually fell to about 100° during the day. Sweating was present and occurred during the late afternoon and night. The child was easily fatigued, but showed interest in her environment and played normally. There was no history of animal contact during the previous two months. She drank pasteurized milk.

PAST HISTORY

The child was born at Garfield Memorial Hospital after a normal, spontaneous delivery. Weight at birth was six pounds and nine ounces. She was bottle fed and had received sufficient cod liver oil and orange juice. She walked at eight months and talked at eighteen months, and had been vaccinated against smallpox and immunized against diphtheria and pertussis. There had been no childhood contagious diseases. She had been treated for acute tonsillitis and bilateral otitis media in this hospital about a week before this present illness, and had had influenza and otitis six months before the present illness.

PHYSICAL EXAMINATION

The patient was well-developed and fairly well nourished white girl about four and one-half years old. She appeared chronically ill and was very uncooperative. There were no rashes present or lymphadenopathy. The ears showed bilateral injection of the floor of the canals. Tonsils were slightly hypertrophied. Chest examination revealed diminished resonance and a decrease in breath sounds over the lower lobes bilaterally. The heart was negative except for a possible gallop rhythm. Extremities showed muscle weakness with some flaccidity of the left leg. There was no tenderness, swelling, or redness of the extremities. Reflexes were hyperactive.

Corrected sedimentation rate was 52 mm. One blood culture showed streptococcus anhemolyticus and two succeeding blood cultures showed staphylococcus albus hemolyticus. X-ray of the affected thigh failed to demonstrate osteal or periosteal pathology. The spine was also negative. X-ray of the chest revealed an in-

crease in bronchovascular markings throughout both lung fields. The heart was enlarged to the left and the left border did not present the normal contour. Blood counts showed hemoglobin 9.5 grams, erythrocytes 3,600,000, leucocytes 17,400. Differential: neutrophiles 44%, lymphocytes 51%, and monocytes 5%. The urine showed a trace of albumin, and microscopic examination, a few red and white blood cells.

HOSPITAL COURSE

The pulse varied from 95 to 190 throughout the hospital stay. The temperature fluctuated between normal and 103°. The fever seemed to hit a peak in the late evening. The patient was given sulfadiazine throughout her hospital course.

Eight blood transfusions were given. A suggestive short systolic murmur at the apex developed on the eighteenth day. At the same time, the liver was palpable three fingers below the costal margin.

She was discharged on 5-4-44, almost a month after admission, without a definite diagnosis. Upon dismissal, her temperature was 102° F.

SECOND ADMISSION

The symptoms were essentially the same, but the patient had become definitely worse. There had been a continued loss of weight and fever, increased irritability, pain in the left hip region and a small area of tenderness below the right knee.

The temperature on admission was 105.4° and the pulse rate was 110. A soft apical systolic murmur was still present, the ear drums were injected, the liver was enlarged and tender, and the spleen was palpable. There was marked tenderness over the left hip and right knee, and there were a number of small discrete pink spots over the abdomen. Similar spots were also present over the neck and shoulders. There was an indefinite rounded mass in the left upper quadrant. Rectal examination revealed two hard brown stone-like masses which were removed with ease by the examining finger. Later, the child developed marked dyspnea, with retraction of the intercostal spaces. There was no reaction to light or accommodation of the pupils.

The urine was cloudy, gave an acid reaction; specific gravity 1.026; albumin ten milligrams per hundred cc., and microscopic

examination showed many white blood cells, few coarse granular casts, few sulfa crystals, and rare red cells.

A hemogram revealed eleven grams of hemoglobin, 3,850,000 red cells, 8,800 white cells with a differential count of neutrophiles 38%, lymphocytes 59%, and monocytes 3%. Thrombocyte count was 40,000. Coagulation time was three minutes, and bleeding time was one minute and twenty seconds. Sedimentation rate was 46. Blood culture (2x) showed Staphylococcus albus. Bone marrow smears, from the tibia, were essentially negative. Blood phosphorus was 5.3 mgm. Blood calcium was 11.4 mgm. Acid phosphatase was high normal, and alkaline phosphatase was slightly raised (28 units). Kahn was negative.

A flat plate of the abdomen and an intravenous pyelogram were reported as being normal. Roentgenographic examination of the pelvis, sacrum, coccyx and hips, and the upper thirds of the femora revealed a marked destructive process involving all the pelvic bones and the upper thirds of the femora. Examination of the knee in the antero-posterior and lateral positions revealed destructive areas in both distal ends of the femora, more marked on the left side. X-ray of the shoulder girdles revealed a destructive process of the upper thirds of the humeri, more marked near the surgical necks. There were some disturbances in the architecture of the upper portion of the frontal bones and the upper and anterior portions of the parietal bones. Sternal puncture was negative for evidence of a blood dyscrasia.

She was given daily flood exposures of x-rays to the entire body for about eight days just before her demise, without appreciable benefit. Seven hundred and forty thousand units of penicillin were administered with a subsequent fall in temperature. The child had a steady downhill course however. Pain in the hips increased and the child frequently screamed with pain. Seven blood transfusions were given. She developed severe pains in the abdomen and under the left scapula, which were constant. The abdomen became hard and distended. During the last weeks of life there was difficulty in urination. A blister-like area developed on the lower left leg and a similar lesion later developed over the coccyx. There developed a swelling of the skull in the region of the anterior fontanelle and discoloration of the tissues about the right eye with slight protrusion of the lids. Just before death the child had very labored breathing, glassy eyes, coma, a temperature of 109°, Cheyne-Stokes breathing, and then death.

NECROPSY REPORT—Dr. John Cassidy

The body was that of a well-developed, emaciated, white female child, estimated age six years. There was some protrusion of the right eye with eccymosis of the periorbital tissue and a bluish discoloration of the right side of the face and ear. There were a number of petechial spots varying in size from pin point to pin head over the thorax and abdomen.

On reflecting the scalp a number of soft hemorrhagic areas varying in size from 3 cm. to 4 cm. in diameter were found over the upper portion of the frontal bone, and also over the portions of the parietal bones adjacent to the sagittal suture. These areas showed proliferation of the bone with spicule formation. The right post-orbital region was involved by a metastatic new growth represented by a soft brownish semi-fluid mass of tissue. The ribs showed similar metastatic involvement. Microscopic study of the bone revealed replacement of the normal marrow by neuroblastic tissue.

The brain, heart and lungs showed no significant changes. The lymph nodes about the thoracic aorta were enlarged and microscopic examination revealed a complete replacement of the lymphoid tissue by small, deeply staining round cells, in some areas arranged in rosettes.

The spleen, kidneys, adrenals and pancreas showed no significant changes.

The liver was markedly enlarged, weighing 1940 gms., as compared to an average normal of 640 gms. The surface was somewhat irregular due to the presence of numerous grayish masses which varied in size from pinhead to 5 mm. in diameter. Microscopically, the tissue was seen to be infiltrated by small, deeply staining round cells, many of which are arranged in groups and often showing rosette formation, which is rather typical of neuroblastoma. The central areas of some of these masses showed hemorrhage.

Just above the left kidney was a rather soft irregular retroperitoneal mass, measuring approximately 9 cm. x 5 cm. x 6 cm. This was adjacent to the kidney, but did not involve it. Adjoining the mass were a number of enlarged hemorrhagic lymph nodes. It extended superiorly as far as the pancreas and medially across the vertebral column over the aorta, but did not involve it. The lymph nodes above and below the mass showed metastatic involve-

ment. Microscopically, there was a complete replacement of the lymphoid tissue by neuroblastic tissue, as described above.

PATHOLOGICAL DIAGNOSIS

Neuroblastoma arising from the abdominal sympathetic nervous system with metastases to retroperitoneal and thoracic lymph nodes, liver, meninges, skull, long bones, and right post-orbital region; purpura involving the skin, epicardium, and bladder mucosa; pulmonary edema and atelectasis; hydronephrosis and hydroureter, left.

DISCUSSION—Dr. E. Clarence Rice

The case which has been reported here today represents one in which there was considerable difficulty in making the proper diagnosis. Some of the laboratory findings tended to obscure the diagnosis rather than aid in it. After the tumor mass in the abdomen became palpable the diagnosis of neuroblastoma should have been seriously considered, but apparently was not.

The early manifestations of this disease are often such as to make the solution of the problem a difficult one. In this case the fever, pain in the leg with leucocytosis strongly suggested an infection, possibly an osteomyelitis. The onset of this patient's illness was not unlike that seen in leukemia, Ewing's sarcoma or osteomyelitis. The two most common causes of malignant abdominal tumors in children at this and other Children's Hospitals are neuroblastoma or sympathicoblastoma and Wilm's tumor or embryoma of the kidney. At this hospital, Wilm's tumor has been seen more often, while at the Children's Hospital, in Boston, Ladd and Gross (1) report that neuroblastoma is the most common, forty cases having been reported.

Neuroblastoma occurs most frequently in young children and here has been usually found on the left side of the abdomen. Ladd and Gross have found these tumors to be radiosensitive in several cases while none of ours have been found to be so. In fact, we have used the lack of sensitivity as a means of making a diagnosis since the lymphoblastomas, with which this type of malignancy is sometimes confused, are particularly sensitive to irradiation.

In the past, two types of metastases have been described, viz., the Pepper syndrome starting with a tumor of the sympathetic system metastasizing to the liver and the Hutchinson syndrome

beginning with a similar primary tumor and metastasizing to the orbit and skull as well as other organs and bones. There is no reason why these designations should be used in the future. While these tumors often arise from the adrenals they are more often found to have their beginning from the sympathetic tissue in the thorax or abdomen, most commonly in the latter.

The metastases are often massive and usually extensive, travelling by the lymphaties and blood stream. Lymph nodes are extensively involved and the liver is usually the site of numerous irregularly rounded tumor masses, often hemorrhagic and sometimes undergoing softening within their centers. Not infrequently is the eyeball found to be protruding due to involvement of the orbit. The skull often is the site of tumor masses and the bone shows areas with spicules pressing on the dura with involvement of the latter. Microscopically, all organs are often found to be affected and the bones will show extensive metastases.

Occasionally, the biopsy of a surface lesion causes the pathologist some difficulty in making a diagnosis due to the similarity of the cells to lymphoblasts. The microscopic appearance of the neoplasm is rather characteristic, the cells being similar in appearance to lymphoblasts, and often having a rather characteristic rosette or circular arrangement. This is not always demonstrable. The presence of a fibrillar network, often in the central portions of the rosettes, is characteristic. With proper stains these can be demonstrated to be neurofibrils.

While other tumors such as lymphosarcoma, Hodgkin's granuloma, mesenteric and omental cysts and hydronephrosis are not uncommon, one should always place neuroblastoma and embryoma of the kidney high on the list of the diagnostic possibilities. This was apparently not done in this case and it was not until Captain Wyatt, who has had such an unusual opportunity of studying such cases in Boston, saw the patient and the X-ray films, that the correct diagnosis was suggested.

Reference:

Ladd and Gross, *Abdominal Surgery of Infancy and Childhood*, W. B. Saunders Co., Philadelphia (1941).

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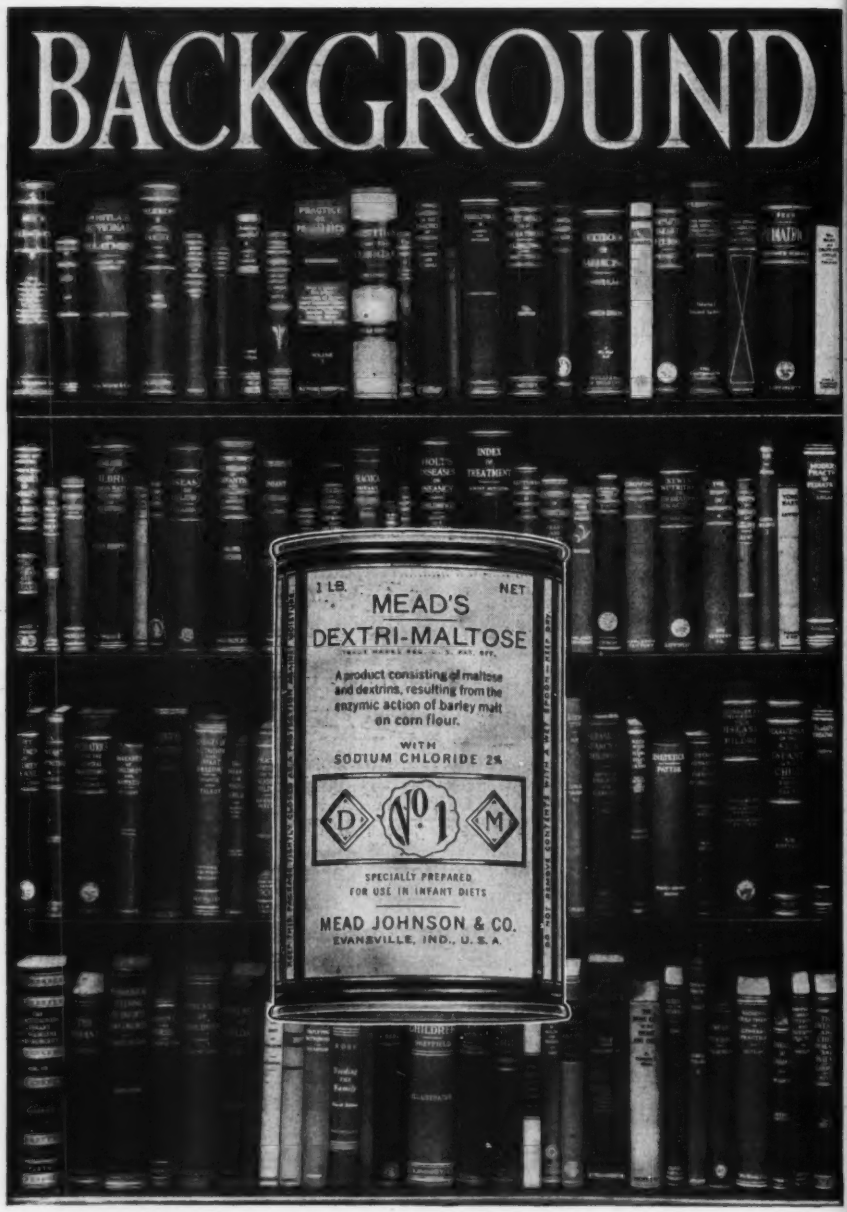
BACKGROUND



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